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Developing Vascular Graft from Adipose-derived Stem Cells

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Opportunity and Significance

Coronary heart disease (CHD) is the most common type of heart disease.[1] One current method used to address CHD is Coronary Artery Bypass Grafting (CABG). CABG is an effective method, with a 95-98% success rate.[1] However, the procedure could be optimized by eliminating the need for the invasive dissection of a healthy vein or artery and the risk of rejection in the cases with a donor vessel.

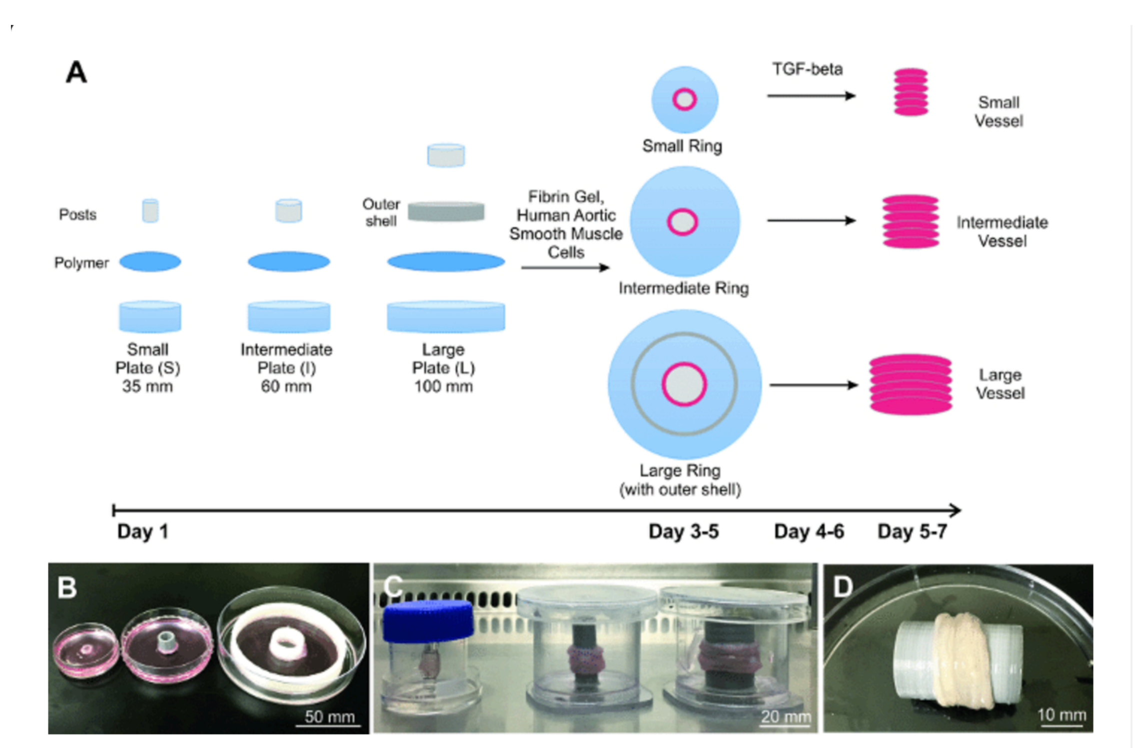
Technical Objectives

This project aims to differentiate Adipose-derived stem cells into fibroblasts through the addition of platelet-derived growth factor (PDGF) into the culture media. Differentiation protocol will be optimized, then successful differentiation will be verified through PCR analysis. The ASC-fibroblasts will then be seeded into a ring construct as outlined by the protocol by Dr. Lam et al.[2] The ring constructs will be tensile tested and analyzed through histology to characterize their strength and cellularity.

Related Work and State of Practice

Dr. Lam's Cardiovascular Regenerative Mechanics Lab has outlined a method with which scalable ring constructs can be formed with polydimethylsiloxane (PDMS) center posts and seeded fibrin hydrogel.[2] This work has been expanded to include 3D-printed inserts as the center posts and has been published in JOVE. Their published work has been done using smooth muscle cells and fibroblasts. This project uses the scalable ring construct method, shown in Figure 1, with ASC-fibroblasts.

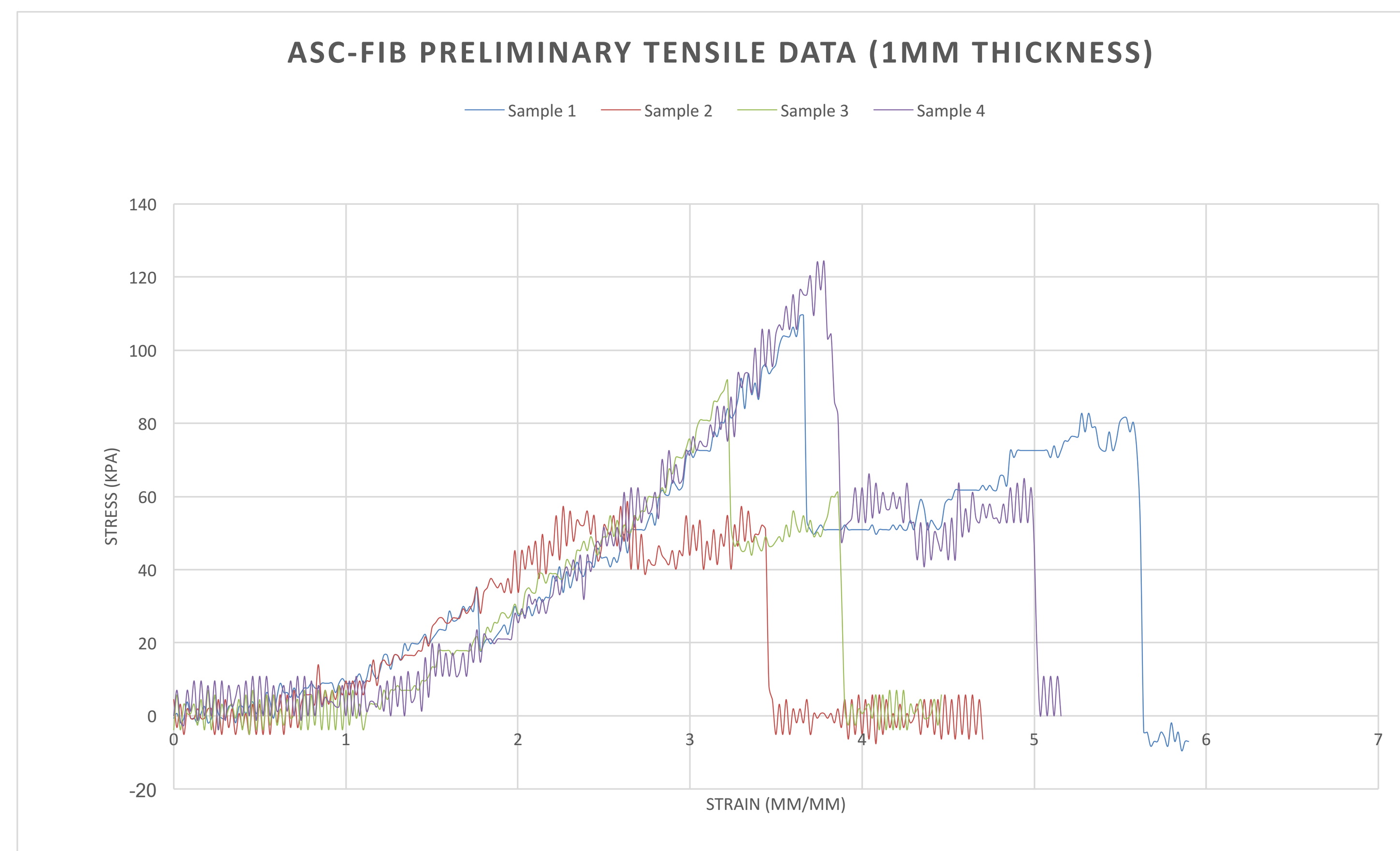
Figure 1: Scalable Ring Construct Method



Technical Approach, Accomplishments and Results

Preliminary tensile data taken during the optimization of seeding parameters are shown in Figure 2. Histology of one ring is shown in Figure 3. ASC's were successfully differentiated into fibroblasts as shown in the PCR data of Figure 4.

Figure 2: Tensile Test Results



Sample (n=4)	E	UTS	FS
1	7.919	109.499	18.144
2	8.540	58.569	12.732
3	8.993	91.673	14.961
4	11.336	124.141	15.597
Average	9.197	95.970	15.358
SDV	1.493	28.248	2.226

Figure 3: H&E stain on one ring 10x magnification

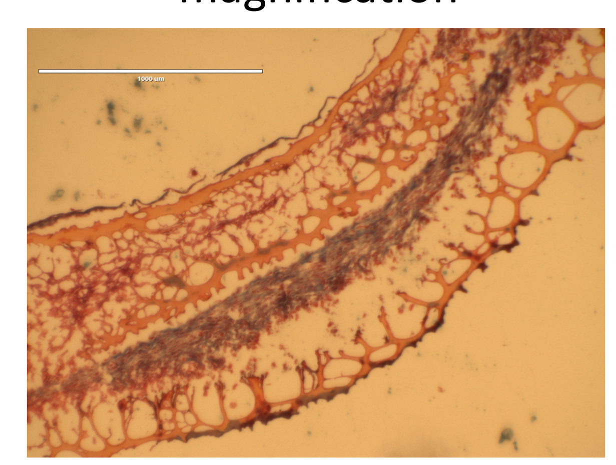
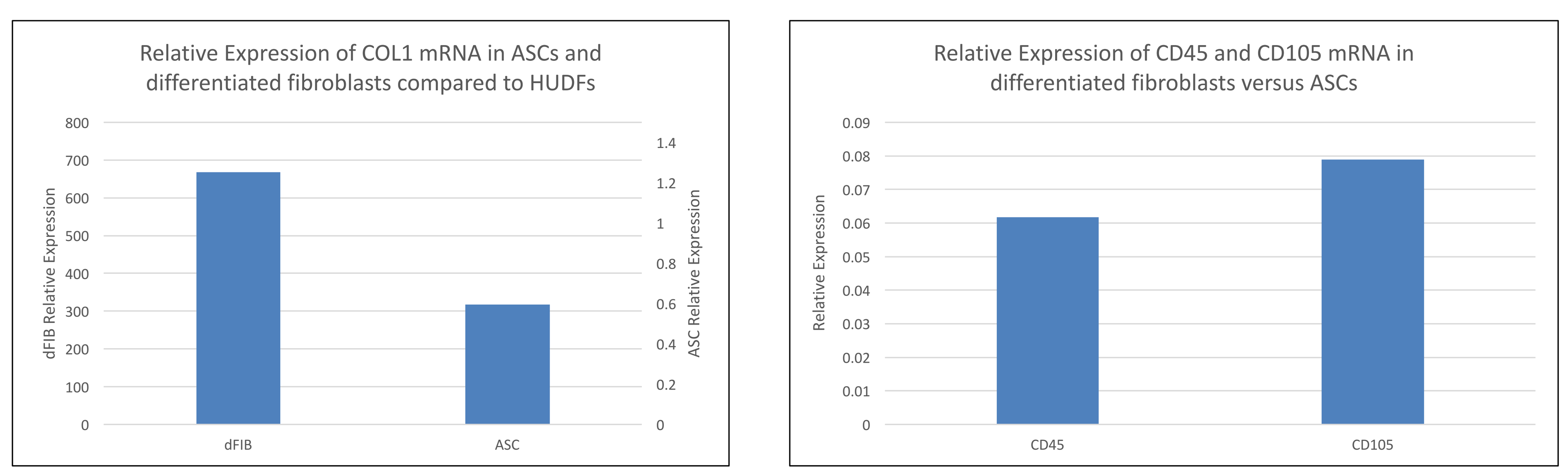


Figure 4: PCR Results



Next Steps for Development and Test

Once the ASC-fibroblast ring constructs are optimized individually for strength and cellularity, the rings will be stacked to form a vascular graft. Tensile testing and histology on the vascular graft will then be done to characterize its strength and the integration of individual rings. Burst pressure will be analyzed to characterize the circumferential strength of the vascular graft, which is essential in validating its functionality.

Commercialization Plan & Partners

This project was done under the guidance of Dr. Lam and in collaboration with Alexander Pietroski and Tannia Rodriguez. We are continuing the work for this project at least through the upcoming Summer and Fall 2018.

The main target consumer for a successful ASC-fibroblast vascular graft would be a cardiovascular surgeon. Dr. Lam's lab communicates frequently with Dr. Kabbani, a cardiovascular surgeon. Moving forward to commercialization, other cardiovascular surgeons would be approached to confirm the handling ability of the vascular grafts. Clinical trials would also have to be conducted in order to validate the long-term durability of the ring constructs prior to commercialization.

References

1. "Coronary Artery Disease (CAD)." *Centers for Disease Control and Prevention*. Centers for Disease Control and Prevention, 10 Aug. 2015. Web. 30 Mar. 2017.
2. Pinnock, Cameron et al. "Customizable Engineered Blood Vessels Using 3D Printed Inserts." Elsevier (2015).

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